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The structure-activity program has received much attention in the past two months with major effort devoted to organizing and coordinating the programs. An additional 50 compounds have been profiled and added to the odor data base. In addition to odorants of general interest, several groups of odorants having similar structures were also evaluated. Thus, 2-, 3- and 4-acylated pyridines were studied in order to understand structural parameters related to popcorn-nutty character. A series of low molecular weight aliphatic acids was studied in an attempt to find out where in the series the trigeminal component of the response disappears and the response becomes purely olfactory. Three other series of compounds, namely, coumarin-like odorants, 1,3-dialkylbenzenes and 2,6-dialkylpyridines were also studied recently¹.

We are continuing our work on terpene esters of pyromellitic acid as resolving agents for alkaloids. Treatment of (R,S)-nicotine with p-di-1-menthyl pyromellitate gave the corresponding R- and S-salts. From the R-salt, (R)-nicotine was obtained in 97.6% e.e., and (S)-nicotine was obtained from the corresponding S-salt in 98.9% e.e. A parallel experiment with the diester derived from d-menthol gave similar results.² Other diesters of pyromellitic acid were prepared. The 1-bornyl diester was reacted with (R,S)-nicotine to give a solid which after a second crystallization was found to yield (S)-nicotine in 95.1% e.e. The (R)-nicotine which was isolated from the mother liquors and had only 78.3% e.e., was crystallized with p-di-1-menthyl pyromellitate to give a diastereomer free of the S-salt. The use of two resolving agents eliminates the need for manual separation of crystals as was required in the case of the 1-menthyl derivative. The use of the diester derived from 1-isopinocampheol for resolving (R,S)-nicotine is in progress.²

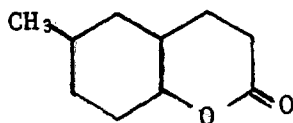
Attempt was made to apply the above new resolving agents to other nicotine derivatives. Thus, the 1-bornyl derived diester was reacted with (R,S)-5-methylnicotine, (R,S)-6-methylnicotine and (R,S)-nornicotine. This work is currently in progress.²

The synthesis of several nicotine analogues has been completed. Thus, 5,6-dimethylnicotine and 6-ethyl-5-methylnicotine were prepared (about 3g of each).

We have renewed our interest in the reaction of some alkylpyrazine anions that can lead to some novel pyrrolopyrazines. Thus, tetramethylpyrazine anion was reacted with pyruvaldehyde dimethylacetal to give the expected alcohol. Experiments to hydrolyze or reduce the acetal function are in progress.²

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The synthesis of 6-methyl-octahydrocoumarine has been completed. The separation of isomers is in progress.³



The strongly fluorescent terbium dipivaloylmethanide was prepared to try to monitor the hydrolytic behaviour of the gadolinium chelate, NaGdEDTA, when applied to tobacco. This research is done in collaboration with Project 2501.

References:

- 1) Rett Southwick, NB #7798
- 2) John Paine, NB #8128
- 3) Mark Sito, NB #8124

Foran Hamlin

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